

Amendments to the Claims:

The following listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Original) An isolated GABA_B receptor protein comprising at least one GABA_BR1a subunit and at least one GABA_BR2 subunit, characterized in that said GABA_B receptor has one high affinity agonist binding site and one low affinity agonist binding site.
2. (Original) The GABA_B receptor protein according to claim 1 wherein the GABA_BR1a subunit is encoded by the oligonucleotide sequence consisting of SEQ ID No.1 and the GABA_BR2 subunit is encoded by the oligonucleotide sequence consisting of SEQ ID N0.3.
3. (Currently Amended) The GABA_B receptor protein according to ~~claims 1 or 2~~claim 1 wherein said receptor protein is expressed by the hGABA_BR1a/GABA_BR2 CHO cell line deposited at the Belgian Coordinated Collections of Microorganisms (BCCM) as CHO-K1 h-GABA-b R1a/R2 clone 20 on August 22, 2003 with the accession number LMBP 6046CB.
4. (Currently Amended) Use of the GABA_B receptor protein according to ~~any one of claims 1 to 3~~claim 1 in a method to identify GABA_B receptor agonists or antagonists.
5. (Original) The hGABA_BR1a/GABA_BR2 CHO cell line deposited at the Belgian Coordinated Collections of Microorganisms (BCCM) as CHO-K1 h-GABA-b R1a/R2 clone on August 22, 2003 with the accession number LMBP 6046CB.

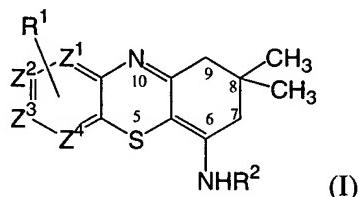
6. (Currently Amended) A method to identify whether a test compound binds to a GABA_B receptor protein according to ~~any one of claims 1 to 3~~claim 1, and is thus a potential agonist or antagonist of the GABA_B receptor, said method comprising:
 - a) contacting cells expressing a functional GABA_B receptor, wherein such cells do not normally express the GABA_B receptor, with the test compound in the presence and absence of a compound known to bind to the GABA_B receptor, and
 - b) determine the binding of the test compound to the GABA_B receptor using the compound known to bind to the GABA_B receptor as a reference.
7. (Original) A method according to claim 6, wherein the compound known to bind to the GABA_B receptor is detectably labeled, and wherein said label is used to determine the binding of the test compound to the GABA_B receptor.
8. (Original) A method according to claim 7 wherein the compound known to bind to the GABA_B receptor is selected from the group consisting of ³H-GABA, ³H-baclofen, ³H-3-APPA, ³H-CGP542626 and ³H-SCH50911.
9. (Original) A method to identify GABA_B receptor agonists said method comprising,
 - a) exposing cells expressing a functional GABA_B receptor, wherein such cells do not normally express the GABA_B receptor, to a labeled agonist of GABA_B in the presence and absence of the test compound, and
 - b) determine the binding of the labeled agonist to said cells,
where if the amount of binding of the labeled agonist is less in the presence of the test compound, then the compound is a potential agonist of the GABA_B receptor.
10. (Original) A method according to claim 10 wherein the labeled agonist is selected from the group consisting of ³H-GABA, ³H-baclofen and ³H-3-APPA.

11. (Original) A method to identify GABA_B receptor antagonists said method comprising,
 - a) exposing cells expressing a functional GABA_B receptor, wherein such cells do not normally express the GABA_B receptor, to a labeled antagonist of GABA_B in the presence and absence of the test compound, and
 - b) determine the binding of the labeled antagonist to said cells,
where if the amount of binding of the labeled antagonist is less in the presence of the test compound, then the compound is a potential antagonist of the GABA_B receptor.
12. (Original) A method according to claim 10 wherein the labeled antagonist is selected from the group consisting of ³H-CPG542626 and ³H-SCH50911.
13. (Original) A method for identifying a compound as a GABA_B receptor agonist, said method comprising;
 - a) administering the compound to a cellular composition of the cells according to claim 5, in the presence of a detectably labeled GABA_B receptor agonist; and
 - b) determine the binding of the labeled agonist to said cellular composition,
where if the amount of binding of the labeled agonist is less in the presence of the test compound, then the compound is a potential agonist of the GABA_B receptor.
14. (Currently Amended) A method according to claim 13 wherein the cellular composition consists of a membrane fraction of the ~~cells according to claim 5~~ hGABA_BR1a/GABA_BR2 CHO cell line deposited at the Belgian Coordinated Collections of Microorganisms (BCCM) as CHO-K1 h-GABA-b R1a/R2 clone on August 22, 2003 with the accession number LMBP 6046CB.

15. (Currently Amended) A method according to ~~claims 13 or 14~~claim 13 wherein the labelled agonist is selected from the group consisting of ^3H -GABA, ^3H -baclofen and ^3H -3-APPA.
16. (Original) A method for identifying a compound as a GABA_B receptor antagonist, said method comprising:
 - a) administering the compound to a cellular composition of the cells according to claim 5, in the presence of a detectably labeled GABA_B receptor antagonist; and
 - b) determine the binding of the labeled antagonist to said cellular composition, where if the amount of binding of the labeled antagonist is less in the presence of the test compound, then the compound is a potential antagonist of the GABA_B receptor.
17. (Currently Amended) A method according to claim 16 wherein the cellular composition consists of a membrane fraction of the ~~cells according to claim 5~~ $\text{hGABA}_\text{B}\text{R1a}/\text{GABA}_\text{B}\text{R2}$ CHO cell line deposited at the Belgian Coordinated Collections of Microorganisms (BCCM) as $\text{CHO-K1 h-GABA-b R1a/R2}$ clone on August 22, 2003 with the accession number LMBP 6046CB.
18. (Currently Amended) A method according to ~~claims 16 or 17~~claim 16 wherein the labeled antagonist is selected from the group consisting of ^3H -CGP542626 and ^3H -SCH50911.
19. (Original) A method for identifying compounds that have the capability to modulate GABA_B receptor activity, said method comprising:
 - a) contacting cells expressing a functional GABA_B receptor, wherein said cells do not normally express a functional GABA_B receptor, with at least one reference compound, under conditions permitting the activation of the GABA_B receptor;
 - b) contacting the cells of step a) with a test compound, under conditions permitting the activation of the GABA_B receptor, and

- c) determine whether said test compound modulates the GABA_B receptor activity compared to the reference compound.
20. (Original) A method according to claim 19 wherein the capability of the test compound to modulate the GABA_B receptor activity is determined using one or more of the functional responses selected from the group consisting of changes in potassium currents, changes in calcium concentration, changes in cAMP and changes in GTP γ S binding
21. (Original) A method for identifying compounds that have the capability to modulate GABA_B receptor activity, said method comprising;
a) contacting a membrane fraction of the cells according to claim 5, with the compound to be tested in the presence of radiolabeld GTP γ S, under conditions permitting the activation of the GABA_B receptor; and
b) determine GTP γ S binding to the membrane fraction,
where an increase in GTP γ S binding in the presence of the compound is an indicaton that the compound activates the GABA_B receptor activity.
22. (Original) A method for identifying compounds that have the capability to modulate GABA_B receptor activity, said method comprising;
a) contacting a membrane fraction of the cells according to claim 5, with the compound to be tested in the presence of radiolabeld GTP γ S, under conditions permitting the activation of the GABA_B receptor; and
b) determine GTP γ S binding to the membrane fraction,
where an decrease in GTP γ S binding in the presence of the compound is an indicaton that the compound inactivates the GABA_B receptor activity.
23. (Currently Amended) A method according to ~~claims 21 or 22~~claim 21 wherein the conditions permitting the activation of the GABA_B receptor comprise the presence of a GABA_B receptor agonist.

24. (Original) A method according to claim 23 wherein the GABA_B receptor agonist is selected from the group consisting of GABA, baclofen and 3-APPA.
25. (Original) Use of a compounds of formula (I)



the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein;
 $=Z^1-Z^2=Z^3-Z^4=$ represents a divalent radical selected from the group consisting of
 $=N-CH=CH-N=$ (a), $=N-CH=N-CH=$ (b), $=CH-N=CH-N=$ (c)
 $=CH-CH=CH-CH=$ (d), $=N-CH=CH-CH=$ (e), $=CH-N=CH-CH=$ (f),
 $=CH-CH=N-CH=$ (g) and $=CH-CH=CH-N=$ (h);
R¹ represents hydrogen, halo, hydroxyl, cyano, C₁₋₆alkyl, CF₃, amino or mono- or di(C₁₋₄alkyl)amino;
R² represents hydrogen, C₁₋₆alkyl or hydroxycarbonyl-C₁₋₆alkyl-, in the manufacture of a medicament for the treatment of an indication such as stiff man syndrome, gastroesophageal reflux, neuropathic pain, incontinence and treatment of cough and cocaine addiction.

26. (Original) Use of a compound of formula (I) in the manufacture of a medicament to reduce transient lower esophageal sphincter relaxations (TLESR).
27. (Original) A compound of formula (I) wherein $=Z^1-Z^2=Z^3-Z^4=$ represents (a), (b) or (d), more preferably those compounds of formula (I) wherein $=Z^1-Z^2=Z^3-Z^4=$ represents (d).
28. (Original) A compound according to claim 27 for use as a medicine.
29. (Original) Use of a compound according to claim 27 in the manufacture of a medicament to reduce transient lower esophageal sphincter relaxations (TLESR).